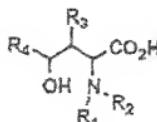


AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

1. (Currently Amended) A method of preparing diastereoisomers and enantiomers of 4-hydroxyisoleucine and derivatives thereof of general formula I



;

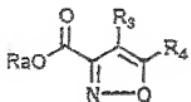
in which R₁ and R₂ represent

· a hydrogen atom or

· one of R₁ or R₂ represents a hydrogen atom and the other substituent is a radical R_a, an acyl group -COR_a, in particular acetyl, or [[else]] a functional group -COOR_a, -SO₂R_a or -N(R_a,R_b), R_a and R_b, which are identical or different, being an optionally substituted linear or branched C1-C12 alkyl radical, an optionally substituted aryl group containing one or more aromatic rings, comprising 5 to 8 C, or aralkyl, wherein the alkyl substituent of said aralkyl is an optionally substituted linear or branched C1-C12 alkyl radical and the aryl group of said aralkyl is an optionally substituted aryl group containing one or more aromatic rings, comprising 5 to 8 Cthe alkyl substituent and the aryl group being as defined above, or

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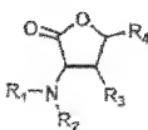
· R₁ and R₂ are the same both represent a substituent as defined above,
said method comprising characterized in that it comprises reducing an
isoxazole derivative of formula II



in which

· R_a is as defined above, and
· R₃ represents a hydrogen atom or R_a, and
· R₄ is an optionally substituted linear or branched C1-C12 alkyl radical, an optionally substituted aryl group containing one or more aromatic rings, comprising 5 to 8 C, or aralkyl, wherein the alkyl substituent of said aralkyl is an optionally substituted linear or branched C1-C12 alkyl radical and the aryl group of said aralkyl is an optionally substituted aryl group containing one or more aromatic rings, comprising 5 to 8 Cthe alkyl substituent and the aryl group being as defined above,

to produce the diastereoisomers and enantiomers of 4-hydroxysoleucine and derivatives thereof of general formula I or to at least one lactone of structure III

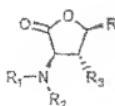


III

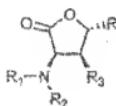
in racemic form(s), or an enantiomerically enriched mixture, followed by the opening, under basic conditions, in a protic or aprotic solvent, of the required lactone or lactones and, optionally if necessary, the separation of the required form.

2. (Original) The method of claim 1, characterized in that the lactone ring is opened by means of LiOH in THF.

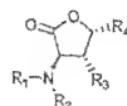
3. (Previously Presented) The method of claim 1, characterized in that the lactone of structure III is obtained by reducing said isoxazole derivative of formula II, leading to a mixture containing 4 lactones L-1, L-2, L-3 and L-4:



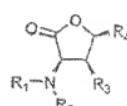
L-1



L-2



L-3



L-4

4. (Original) The method of claim 3, characterized in that, where R₃ represents a hydrogen atom in the isoxazole of formula II, a group R_a is introduced subsequently into

the intermediates obtained.

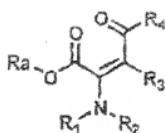
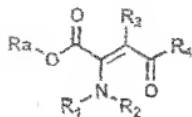
5. (Previously Presented) The method of claim 1, characterized in that the desired lactone or lactones is or are separated in racemic or in enantiomerically pure form, the preparation of one of the lactones and/or one of the enantiomers being promoted by the catalyst and the conditions that are used.

6. (Currently Amended) The method of claim 1, characterized in that the lactones in which R₁ and/or R₂ represent a hydrogen atom are substituted, in particular alkylated, carbamylated, sulfonylated or acylated, especially acetylated.

7. (Previously Presented) The method of claim 1, characterized in that it comprises reducing an isoxazole of formula II in which OR_a represents a hydrogenolysable group.

8. (Previously Presented) The method of claim 1, characterized in that the intermediates formed during the step of reducing the isoxazole derivative of formula II are isolated.

9. (Previously Presented) The method of claim 3, characterized in that operation takes place in an ethanol/water medium, to which a solution of Raney nickel in ethanol and the isoxazole derivative of formula II are added, and the mixture is purged with hydrogen, the reaction medium being subsequently stirred under a hydrogen pressure of the order of 1 atmosphere at ambient temperature, giving the derivatives IV and V:



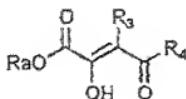
10. (Original) The method of claim 9, characterized in that the compound V is subjected to the action of a reduction catalyst in a solvent in the presence of a hydrogen source.

11. (Original) The method of claim 9, characterized in that the compound IV or V is subjected to the action of a homogeneous reduction catalyst, of a chiral or achiral ligand, in the presence of an organic solvent, of triethylamine and a hydrogen source, or, alternatively, the compounds IV or V are subjected to reduction in an ethanol/water mixture in the presence of NaBH₄ and CeCl₃·7H₂O.

12. (Previously Presented) The method of claim 1, characterized in that the

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isoxazole derivative of formula II is obtained by reacting a hydroxylamine with a 4-keto-2-hydroxy-2-butenoic acid derivative of formula VI:

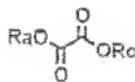


VI

13. (Original) The method of claim 12, characterized in that the 4-keto-2-hydroxy-2-butenoic acid derivative is obtained by condensing a ketone VII and an oxalate derivative VIII:



VII



VIII

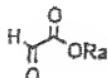
in these formulae, R₅ represents an alkyl, such as ethyl or methyl,

alkylaryl, vinyl or substituted vinyl radical, R_4 and R_a are as defined above. R_c exhibits the significations given by R_a and may be identical to or different from R_a .

14. (Original) The method of claim 13, characterized in that the ketone used is butanone.

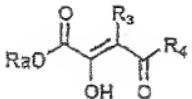
15. (Original) The method of claim 13, characterized in that the ketone used is acetone, leading to the 4-keto-2-hydroxy-2-butenoic acid derivative of formula VI in which R_3 is a hydrogen atom and R_4 represents CH_3 .

16. (Original) The method of claim 13, characterized in that the 4-keto-2-hydroxy-2-butenoic acid of formula VI is obtained by operating in accordance with the Baylis-Hillmann reaction, by reacting methyl vinyl ketone with a glyoxalate of formula IX,



IX

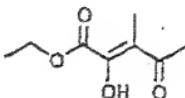
followed either by a step of isomerization to compound VI, in the presence of transition metal catalyst, or by reduction of the double bond and then oxidation of the OH function.



VI

17. (Previously Presented) A method of preparing (2S, 3R, 4S)-4-hydroxyisoleucine, characterized in that it comprises the steps of

- a) synthesis of an ester of pent-2-enoic acid of formula X

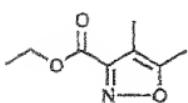


X

either by reacting butanone with ethyl oxalate or by condensing methyl vinyl ketone with ethyl glyoxalate, followed, without purification, by an isomerization reaction or by a reduction/oxidation sequence;

- b) the ester of pent-2-enoic acid obtained reacts with hydroxylamine to form the isoxazole derivative of formula XI,

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XI

- c) the reduction of the isoxazole derivative obtained to give the lactones I-1 to I-4,



I-1



I-2

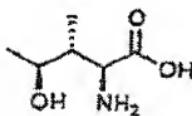


I-3



I-4

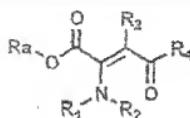
- d) the separation of lactone I-1 to I-4 in racemic form, followed by
- e) the separation of the enantiomer,
- f) the opening of the lactone ring, leading to the compound A



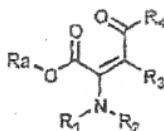
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18. (Currently Amended) A As new products,

the intermediate compound[[s]] of formulae IV [[and]]or V, or C-1, or C-2,
or E-1, or E-2, of the following formula:

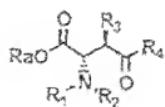


IV

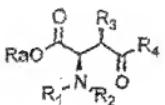


V

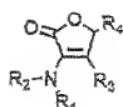
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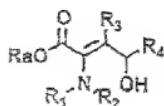
C-1



C-2



E-1



E-2

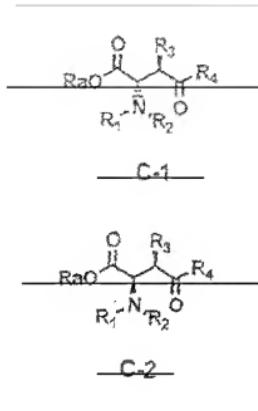
in which one of R₁ and R₂ represents H, and the other substituent is a radical R_a, an acyl group -COR_a, in particular acetyl, or [[else]] a functional group -COOR_a, -SO₂R_a or -N(R_a,R_b), R_a and R_b, which are identical or different, being an optionally substituted linear or branched C1-C12 alkyl radical, an optionally substituted aryl group containing one or more aromatic rings, comprising 5 to 8 C, or aralkyl, wherein the alkyl substituent of said aralkyl is an optionally substituted linear or branched C1-C12 alkyl radical and the aryl group of said aralkyl is an optionally substituted aryl group containing one or more aromatic rings, comprising 5 to 8 C being as defined above,

R₃ represents a hydrogen atom or R_a, and

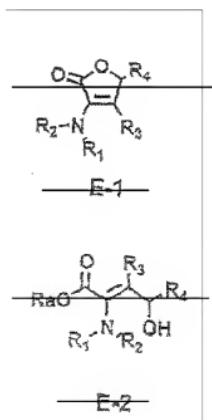
R₄ is an optionally substituted linear or branched C1-C12 alkyl radical, an optionally substituted aryl group containing one or more aromatic rings, comprising 5 to 8 C, or aralkyl, wherein the alkyl substituent of said aralkyl is an optionally substituted linear or branched C1-C12 alkyl radical and the aryl group of said aralkyl is an optionally substituted aryl group containing one or more aromatic rings, comprising 5 to 8 C

— the compounds corresponding to C-1 and C-2, of formulae

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the compounds E-1 and E-2, corresponding to the formulae



in which the substituents are as defined above in relation to the formulae

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IV and V.

19. (new) The method of claim 1 wherein R_a is acetyl.
20. (new) The method of claim 6 wherein said substituted lactones are alkylated carboxylated, sulfonylated or acylated.
21. (new) The method of claim 6 wherein said substituted lactones are acetylated.
22. (new) The method of claim 13 wherein R₅ represents ethyl or methyl.
23. (new) The compound of claim 18 wherein R_a is acetyl.